

SEQUENCE LISTING

<110> Fujisawa Pharmaceutical Co., Ltd. Matsuoka, Hideaki Fujimura, Takao Hayashi, Masako Aramori, Ichiro	
<120> New methods for selecting an immunosuppressive agent	
<130> 274130US0PCT <140> 10/540,546 <141> 2005-06-24	
<150> JP2002-378800 <151> 2002-12-27	
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gat gtg gcc acg gcg ctg cct ctg caa gtg gcc ccc tcg gca gtg ccc Asp Val Ala Thr Ala Leu Pro Leu Gln Val Ala Pro Ser Ala Val Pro 35 40 45	144
atg gac ctg cgc ctg gac cac cag ttc tca ctg cct gtg gca gag ccg Met Asp Leu Arg Leu Asp His Gln Phe Ser Leu Pro Val Ala Glu Pro 50 55 60	192
gcc ctg cgg gag cag cag ctg cag gag ctc ctg gcg ctc aag cag Ala Leu Arg Glu Gln Gln Leu Gln Glu Leu Leu Ala Leu Lys Gln 65 70 75 80	240
aag cag cag atc cag agg cag atc ctc atc gct gag ttc cag agg cag Lys Gln Gln Ile Gln Arg Gln Ile Leu Ile Ala Glu Phe Gln Arg Gln 85 90 95	288
cac gag cag ctc tcc cgg cag cac gag gcg cag ctc cac gag cac atc His Glu Gln Leu Ser Arg Gln His Glu Ala Gln Leu His Glu His Ile 100 105 110	336
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Lys	Gln	Gln 115	Gln	Glu	Met	Leu	Ala 120	Met	Lys	His	Gln	Gln 125	Glu	Leu	Leu	
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						aag Lys										480
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gac · Asp						gcc Ala 295										912
aac Asn 305	agc Ser	tcc Ser	gjà aaa	agc Ser	gtc Val 310	agc Ser	gcg Ala	gag Glu	aac Asn	ggt Gly 315	atc Ile	gcg Ala	ccc Pro	gcc Ala	gtc Val 320	960
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aac Asn	atc Ile	acg Thr	ctg Leu	ggc Gly	ctg Leu	cct Pro	gcc Ala	acc Thr	ggc Gly	ccc Pro	tct Ser	gcg Ala	ggc Gly	acg Thr	gcg Ala	1104

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gag cca Glu Pro													1584
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gag ccg ggc cag cgc cag ccc agt gag cag gag ctg ctc ttc aga cag

Glu Pro Gly Gln Arg Gln Pro Ser Glu Gln Glu Leu Leu Phe Arg Gln

caa gcc ctc ctg ctg gag cag cag cgg atc cac cag ctg agg aac tac

Gln Ala Leu Leu Glu Gln Gln Arg Ile His Gln Leu Arg Asn Tyr

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		ctg Leu														:	1920
		gtg Val														:	1968
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		acc Thr					_	_			_	_	_			:	2160
		tat Tyr														2	2208
		cta Leu														2	2256
		ggg Gly 755														2	2304
		gcc Ala														2	2352
		aca Thr														2	2400
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tcc Ser	gtg Val	gcc Ala	gtg Val 820	gca Ala	gcc Ala	aag Lys	ctt Leu	ctg Leu 825	cag Gln	cag Gln	agg Arg	ttg Leu	agc Ser 830	gtg Val	agc Ser	2	2496
		ctc Leu 835														2	2544

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					gac Asp											2592
tac Tyr 865	gac Asp	gat Asp	Gly aaa	aac Asn	ttc Phe 870	ttc Phe	cca Pro	ggc Gly	agc Ser	999 Gly 875	gct Ala	cct Pro	gat Asp	gag Glu	gtg Val 880	2640
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					atg Met											2736
					atc Ile											2784
gtg Val	tca Ser 930	tca Ser	ggc gly	ttc Phe	gat Asp	gcc Ala 935	gtg Val	gag Glu	ggc Gly	cac His	ccc Pro 940	acc Thr	cct Pro	ctt Leu	gj aaa	2832
					gcc Ala 950											2880
					ggc Gly											2928
					tgc Cys											2976
					gat Asp			Pro					Gln			3024
		Ala			gtc Val		Ser			Lys						3072
	Lys				tgc Cys 1030	Leu					Ser					3120
					cag Gln					Glu					Val	3168
acc Thr	gcc Ala	atg Met	gcc Ala 1060	Ser	ctg Leu	tcc Ser	gtg Val	ggc Gly 1065	Val	aag Lys	ccc Pro	gcc Ala	gaa Glu 1070	Lys	aga Arg	3216
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<212> PRT

<213> Homo sapiens

<400> 2

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Asp Val Ala Thr Ala Leu Pro Leu Gln Val Ala Pro Ser Ala Val Pro 35 40 45

Met Asp Leu Arg Leu Asp His Gln Phe Ser Leu Pro Val Ala Glu Pro 50 55 60

Ala Leu Arg Glu Gln Gln Leu Gln Gln Glu Leu Leu Ala Leu Lys Gln 65 70 75 80

Lys Gln Gln Ile Gln Arg Gln Ile Leu Ile Ala Glu Phe Gln Arg Gln
85 90 95

His Glu Gln Leu Ser Arg Gln His Glu Ala Gln Leu His Glu His Ile 100 105 · 110

Lys Gln Gln Glu Met Leu Ala Met Lys His Gln Gln Glu Leu Leu 115 120 125

Glu His Gln Arg Lys Leu Glu Arg His Arg Gln Glu Gln Glu Leu Glu 130 135 140

Lys Gln His Arg Glu Gln Lys Leu Gln Gln Leu Lys Asn Lys Glu Lys 145 150 155 160

Gly Lys Glu Ser Ala Val Ala Ser Thr Glu Val Lys Met Lys Leu Gln
165 170 175

Glu Phe Val Leu Asn Lys Lys Lys Ala Leu Ala His Arg Asn Leu Asn 180 185 190

His Cys Ile Ser Ser Asp Pro Arg Tyr Trp Tyr Gly Lys Thr Gln His 195 200 205

Ser Ser Leu Asp Gln Ser Ser Pro Pro Gln Ser Gly Val Ser Thr Ser 210 220

Tyr Asn His Pro Val Leu Gly Met Tyr Asp Ala Lys Asp Asp Phe Pro 225 230 235 240

Leu Arg Lys Thr Ala Ser Glu Pro Asn Leu Lys Leu Arg Ser Arg Leu 245 250 255

Lys Gln Lys Val Ala Glu Arg Arg Ser Ser Pro Leu Leu Arg Arg Lys
260 265 270

Asp Gly Pro Val Val Thr Ala Leu Lys Lys Arg Pro Leu Asp Val Thr 275 280 285

Asp Ser Ala Cys Ser Ser Ala Pro Gly Ser Gly Pro Ser Ser Pro Asn

290 295 300
sn Ser Ser Gly Ser Val Ser Ala Glu Asn Gly Ile

Asn Ser Ser Gly Ser Val Ser Ala Glu Asn Gly Ile Ala Pro Ala Val 305

Pro Ser Ile Pro Ala Glu Thr Ser Leu Ala His Arg Leu Val Ala Arg 325

330

335

Glu Gly Ser Ala Ala Pro Leu Pro Leu Tyr Thr Ser Pro Ser Leu Pro 340 345 350

Asn Ile Thr Leu Gly Leu Pro Ala Thr Gly Pro Ser Ala Gly Thr Ala 355 360 365

Gly Gln Gln Asp Thr Glu Arg Leu Thr Leu Pro Ala Leu Gln Gln Arg 370 375 380

Leu Ser Leu Phe Pro Gly Thr His Leu Thr Pro Tyr Leu Ser Thr Ser 385 390 395 400

Pro Leu Glu Arg Asp Gly Gly Ala Ala His Ser Pro Leu Leu Gln His 405 410 415

Met Val Leu Leu Glu Gln Pro Pro Ala Gln Ala Pro Leu Val Thr Gly
420 425 430

Leu Gly Ala Leu Pro Leu His Ala Gln Ser Leu Val Gly Ala Asp Arg
435
440
445

Val Ser Pro Ser Ile His Lys Leu Arg Gln His Arg Pro Leu Gly Arg 450 455 460

Thr Gln Ser Ala Pro Leu Pro Gln Asn Ala Gln Ala Leu Gln His Leu 465 470 475 480

Val Ile Gln Gln His Gln Gln Phe Leu Glu Lys His Lys Gln Gln 485 490 495

Phe Gln Gln Gln Leu Gln Met Asn Lys Ile Ile Pro Lys Pro Ser 500 505 510

Glu Pro Ala Arg Gln Pro Glu Ser His Pro Glu Glu Thr Glu Glu Glu 515 520 525

Leu Arg Glu His Gln Ala Leu Leu Asp Glu Pro Tyr Leu Asp Arg Leu 530 535 540

Pro Gly Gln Lys Glu Ala His Ala Gln Ala Gly Val Gln Val Lys Gln 545 550 555 560

Glu Pro Ile Glu Ser Asp Glu Glu Glu Ala Glu Pro Pro Arg Glu Val
565 570 575

Glu Pro Gly Gln Arg Gln Pro Ser Glu Gln Glu Leu Leu Phe Arg Gln 580 . 585 590

Gln Ala Leu Leu Glu Gln Gln Arg Ile His Gln Leu Arg Asn Tyr 595 600 605

Gln Ala Ser Met Glu Ala Ala Gly Ile Pro Val Ser Phe Gly Gly His 610 615 620

Arg Pro Leu Ser Arg Ala Gln Ser Ser Pro Ala Ser Ala Thr Phe Pro Val Ser Val Gln Glu Pro Pro Thr Lys Pro Arg Phe Thr Thr Gly Leu 650 Val Tyr Asp Thr Leu Met Leu Lys His Gln Cys Thr Cys Gly Ser Ser 665 Ser Ser His Pro Glu His Ala Gly Arg Ile Gln Ser Ile Trp Ser Arg 680 Leu Gln Glu Thr Gly Leu Arg Gly Lys Cys Glu Cys Ile Arg Gly Arg 695 Lys Ala Thr Leu Glu Glu Leu Gln Thr Val His Ser Glu Ala His Thr 710 715 Leu Leu Tyr Gly Thr Asn Pro Leu Asn Arg Gln Lys Leu Asp Ser Lys 725 730 Lys Leu Leu Gly Ser Leu Ala Ser Val Phe Val Arg Leu Pro Cys Gly 745 Gly Val Gly Val Asp Ser Asp Thr Ile Trp Asn Glu Val His Ser Ala 760 Gly Ala Ala Arg Leu Ala Val Gly Cys Val Val Glu Leu Val Phe Lys 775 Val Ala Thr Gly Glu Leu Lys Asn Gly Phe Ala Val Val Arg Pro Pro Gly His His Ala Glu Glu Ser Thr Pro Met Gly Phe Cys Tyr Phe Asn Ser Val Ala Val Ala Ala Lys Leu Leu Gln Gln Arg Leu Ser Val Ser 825 Lys Ile Leu Ile Val Asp Trp Asp Val His His Gly Asn Gly Thr Gln Gln Ala Phe Tyr Ser Asp Pro Ser Val Leu Tyr Met Ser Leu His Arg 855 Tyr Asp Asp Gly Asn Phe Phe Pro Gly Ser Gly Ala Pro Asp Glu Val Gly Thr Gly Pro Gly Val Gly Phe Asn Val Asn Met Ala Phe Thr Gly 890 Gly Leu Asp Pro Pro Met Gly Asp Ala Glu Tyr Leu Ala Ala Phe Arg Thr Val Val Met Pro Ile Ala Ser Glu Phe Ala Pro Asp Val Val Leu 920 Val Ser Ser Gly Phe Asp Ala Val Glu Gly His Pro Thr Pro Leu Gly 935 940

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Asj) Leu	Thr	Ala 980	Ile	Cys	Asp	Ala	Ser 985	Glu	Ala	Cys	Val	Ser 990	Ala	Leu	
Le	ı Gly	Asn 995	Glu	Leu	Asp	Pro	Leu 1000		Glu	Lys	Val	Leu 100		Gln	Arg	
Pro	Asn 101		Asn	Ala	Val	Arg 101		Met	Glu	Lys	Val 1020		Glu	Ile	His	
Se:	Lys 25	Tyr	Trp	Arg	Cys 1030		Gln	Arg	Thr	Thr 103		Thr	Ala	Gly	Arg 1040)
Se	Leu	Ile	Glu	Ala 1049		Thr	Cys	Glu	Asn 1050		Glu	Ala	Glu	Thr 105		
Th	Ala	Met	Ala 1060		Leu	Ser	Val	Gly 1065		Lys	Pro	Ala	Glu 1070	_	Arg	
Pro	Asp	Glu 107		Pro	Met	Glu	Glu 1080		Pro	Pro	Leu					
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	gtg Val															144
	gac : Asp 50															192
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Lys	Gln	Gln	Ile	Gln 85	Arg	Gln	Ile	Leu	Ile 90	Ala	Glu	Phe	Gln	Arg 95	Gln	
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						aag Lys										480
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gaa Glu	ttt Phe	gtc Val	ctc Leu 180	aat Asn	aaa Lys	aag Lys	aag Lys	gcg Ala 185	ctg Leu	gcc Ala	cac His	cgg Arg	aat Asn 190	ctg Leu	aac Asn	576
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						aga Arg										816
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						agc Ser										960
						acg Thr										1008

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gaa gg Glu G		_	_	_						_			_		1056
aac at Asn I	le '	_	_		_		_						_		1104
Gly G	_	_	-			_				_		_	_		1152
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ccc to Pro Le															1248
atg gi Met Va															1296
ctg gg Leu G	ly .														1344
gtg to Val Se 4!						_	_	 _		_		_			1392
acc ca Thr G															1440
gtc at Val I		_	_	_		_	_	_	_			_	_	_	1488
ttc ca															1536
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ctc co Leu Ar 53															1632
ccg gg Pro G															1680
gag co Glu Pi															1728

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					gag Glu											1824
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					ccc Pro											1968
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					ctc Leu											2112
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					aac Asn											2208
					ctc Leu											2256
					agt Ser											2304
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								ctg Leu 825								2496
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								ttc Phe								2880
								gtc Val								2928
								tcg Ser 985								2976
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		Ala					Ser	atg Met				Met				3072
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Thr Ala Met Ala Ser Leu Ser Val Gly Val Lys Pro Ala Glu Lys Arg 1060 1065 1070

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<210> 4

<211> 1084

<212> PRT

<213> Artificial Sequence

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<223> Dominant negative mutant (H802K, H803L) of human histone deacetylase-4 (HDAC4) gene

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Asp Val Ala Thr Ala Leu Pro Leu Gln Val Ala Pro Ser Ala Val Pro 35 40 45

Met Asp Leu Arg Leu Asp His Gln Phe Ser Leu Pro Val Ala Glu Pro 50 55 60

Ala Leu Arg Glu Gln Gln Leu Gln Glu Leu Leu Ala Leu Lys Gln 65 70 75 80

Lys Gln Gln Ile Gln Arg Gln Ile Leu Ile Ala Glu Phe Gln Arg Gln 85 90 95

His Glu Gln Leu Ser Arg Gln His Glu Ala Gln Leu His Glu His Ile
100 105 110

Lys Gln Gln Gln Glu Met Leu Ala Met Lys His Gln Gln Glu Leu Leu 115 120 125

Glu His Gln Arg Lys Leu Glu Arg His Arg Gln Glu Gln Glu Leu Glu 130 135 140

Lys Gln His Arg Glu Gln Lys Leu Gln Gln Leu Lys Asn Lys Glu Lys 145 150 155 160

Gly Lys Glu Ser Ala Val Ala Ser Thr Glu Val Lys Met Lys Leu Gln 165 170 175

Glu Phe Val Leu Asn Lys Lys Lys Ala Leu Ala His Arg Asn Leu Asn 180 185 190

His Cys Ile Ser Ser Asp Pro Arg Tyr Trp Tyr Gly Lys Thr Gln His
195 200 205

Ser Ser Leu Asp Gln Ser Ser Pro Pro Gln Ser Gly Val Ser Thr Ser 210 215 220

Tyr Asn His Pro Val Leu Gly Met Tyr Asp Ala Lys Asp Asp Phe Pro Leu Arg Lys Thr Ala Ser Glu Pro Asn Leu Lys Leu Arg Ser Arg Leu 250 Lys Gln Lys Val Ala Glu Arg Arg Ser Ser Pro Leu Leu Arg Arg Lys 265 Asp Gly Pro Val Val Thr Ala Leu Lys Lys Arg Pro Leu Asp Val Thr 280 Asp Ser Ala Cys Ser Ser Ala Pro Gly Ser Gly Pro Ser Ser Pro Asn 295 Asn Ser Ser Gly Ser Val Ser Ala Glu Asn Gly Ile Ala Pro Ala Val 310 315 Pro Ser Ile Pro Ala Glu Thr Ser Leu Ala His Arg Leu Val Ala Arg 325 330 Glu Gly Ser Ala Ala Pro Leu Pro Leu Tyr Thr Ser Pro Ser Leu Pro 345 Asn Ile Thr Leu Gly Leu Pro Ala Thr Gly Pro Ser Ala Gly Thr Ala 360 Gly Gln Gln Asp Thr Glu Arg Leu Thr Leu Pro Ala Leu Gln Gln Arg 375 Leu Ser Leu Phe Pro Gly Thr His Leu Thr Pro Tyr Leu Ser Thr Ser 390 395 Pro Leu Glu Arg Asp Gly Gly Ala Ala His Ser Pro Leu Leu Gln His 410 Met Val Leu Leu Glu Gln Pro Pro Ala Gln Ala Pro Leu Val Thr Gly 425 Leu Gly Ala Leu Pro Leu His Ala Gln Ser Leu Val Gly Ala Asp Arg Val Ser Pro Ser Ile His Lys Leu Arg Gln His Arg Pro Leu Gly Arg Thr Gln Ser Ala Pro Leu Pro Gln Asn Ala Gln Ala Leu Gln His Leu 475 Val Ile Gln Gln His Gln Gln Phe Leu Glu Lys His Lys Gln Gln Phe Gln Gln Gln Leu Gln Met Asn Lys Ile Ile Pro Lys Pro Ser 505 Glu Pro Ala Arg Gln Pro Glu Ser His Pro Glu Glu Thr Glu Glu Glu Leu Arg Glu His Gln Ala Leu Leu Asp Glu Pro Tyr Leu Asp Arg Leu Pro Gly Gln Lys Glu Ala His Ala Gln Ala Gly Val Gln Val Lys Gln

545					550					555					560
Glu	Pro	Ile	Glu	Ser 565	Asp	Glu	Glu	Glu	Ala 570	Glu	Pro	Pro	Arg	Glu 575	Val
Glu	Pro	Gly	Gln 580	Arg	Gln	Pro	Ser	Glu 585	Gln	Glu	Leu	Leu	Phe 590	Arg	Gln
Gln	Ala	Leu 595	Leu	Leu	Glu	Gln	Gln 600	Arg	Ile	His	Gln	Leu 605	Arg	Asn	Tyr
Gln	Ala 610	Ser	Met	Glu	Ala	Ala 615	Gly	Ile	Pro	Val	Ser 620	Phe	Gly	Gly	His
Arg 625	Pro	Leu	Ser	Arg	Ala 630	Gln	Ser	Ser	Pro	Ala 635	Ser	Ala	Thr	Phe	Pro 640
Val	Ser	Val	Gln	Glu 645	Pro	Pro	Thr	Lys	Pro 650	Arg	Phe	Thr	Thr	Gly 655	Leu
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		675					Gly 680					685	_		
Leu	Gln 690	Glu	Thr	Gly	Leu	Arg 695	Gly	Lys	Cys	Glu	Cys 700	Ile	Arg	Gly	Arg
Lys 705	Ala	Thr	Leu	Glu	Glu 710	Leu	Gln	Thr	Val	His 715	Ser	Glu	Ala	His	Thr 720
Leu	Leu	Tyr	Gly	Thr 725	Asn	Pro	Leu	Asn	Arg 730	Gln	Lys	Leu	Asp	Ser 735	Lys
Lys	Leu	Leu	Gly 740	Ser	Leu	Ala	Ser	Val 745	Phe	Val	Arg	Leu	Pro 750	Сув	Gly
_		755		_		_	Thr 760		_			765			
Gly	Ala 770	Ala	Arg	Leu	Ala	Val 775	Gly	Cys	Val	Val	Glu 780	Leu	Val	Phe	Lys
Val 785	Ala	Thr	Gly	Glu	Leu 790	Lys	Asn	Gly	Phe	Ala 795\	Val	Val	Arg	Pro	Pro 800
Gly	Lys	Leu	Ala	Glu 805	Glu	Ser	Thr	Pro	Met 810	Gly	Phe	Cys	Tyr	Phe 815	Asn
Ser	Val	Ala	Val 820	Ala	Ala	Lys	Leu	Leu 825	Gln	Gln	Arg	Leu	Ser 830	Val	Ser
		835					Asp 840				_	845	_		
	850					855	Ser				860				
Tyr 865	Asp	Asp	Gly	Asn	Phe 870	Phe	Pro	Gly	Ser	Gly 875	Ala	Pro	Asp	Glu	Val 880

Gly Thr Gly Pro Gly Val Gly Phe Asn Val Asn Met Ala Phe Thr Gly Gly Leu Asp Pro Pro Met Gly Asp Ala Glu Tyr Leu Ala Ala Phe Arg 905 Thr Val Val Met Pro Ile Ala Ser Glu Phe Ala Pro Asp Val Val Leu 920 Val Ser Ser Gly Phe Asp Ala Val Glu Gly His Pro Thr Pro Leu Gly 935 Gly Tyr Asn Leu Ser Ala Arg Cys Phe Gly Tyr Leu Thr Lys Gln Leu 950 955 Met Gly Leu Ala Gly Gly Arg Ile Val Leu Ala Leu Glu Gly Gly His 965 970 Asp Leu Thr Ala Ile Cys Asp Ala Ser Glu Ala Cys Val Ser Ala Leu 985 Leu Gly Asn Glu Leu Asp Pro Leu Pro Glu Lys Val Leu Gln Gln Arg 1000 Pro Asn Ala Asn Ala Val Arg Ser Met Glu Lys Val Met Glu Ile His 1015 Ser Lys Tyr Trp Arg Cys Leu Gln Arg Thr Thr Ser Thr Ala Gly Arg Ser Leu Ile Glu Ala Gln Thr Cys Glu Asn Glu Glu Ala Glu Thr Val 1050 Thr Ala Met Ala Ser Leu Ser Val Gly Val Lys Pro Ala Glu Lys Arg 1060 Pro Asp Glu Glu Pro Met Glu Glu Pro Pro Leu 1080 <210> 5 <211> 3255 <212> DNA <213> Artificial Sequence <220> <221> CDS <222> (1)..(3255) <223> Dominant negative mutant (H863L) of human histone deacetylase-4 (HDAC4) gene <400> 5 atg age tee caa age cat eea gat gga ett tet gge ega gae eag eea 48 Met Ser Ser Gln Ser His Pro Asp Gly Leu Ser Gly Arg Asp Gln Pro gtg gag ctg ctg aat cct gcc cgc gtg aac cac atg ccc agc acg gtg 96 Val Glu Leu Leu Asn Pro Ala Arg Val Asn His Met Pro Ser Thr Val 20 25

					caa Gln					144
					ttc Phe					192
					cag Gln					240
					ctc Leu				cag Gln	288
					gag Glu 105					336
					atg Met					384
					cac His					432
					cag Gln					480
					aca Thr					528
					gcg Ala 185					576
					tac Tyr				cac His	624
					ccc Pro					672
					tac Tyr					720
			_	_	aat Asn	_				768
					agc Ser 265					816

														gtc Val		864
														ccc Pro		912
														gcc Ala		960
														gca Ala 335		1008
_		_	_	_							_			ttg Leu		1056
		_	_		_		_							acg Thr		1104
														cag Gln		1152
												_	_	acc Thr	_	1200
ccc Pro	ttg Leu	gag Glu	cgg Arg	gac Asp 405	gga Gly	GJÀ aaa	gca Ala	gcg Ala	cac His 410	agc Ser	cct Pro	ctt Leu	ctg Leu	cag Gln 415	cac His	1248
														aca Thr		1296
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														Gly aaa		1392
														cac His		1440
														cag Gln 495		1488
														cca Pro		1536
gag	cca	gcc	cgg	cag	ccg	gag	agc	cac	ccg	gag	gag	acg	gag	gag	gag	1584

Glu	Pro	Ala 515	Arg	Gln	Pro	Glu	Ser 520	His	Pro	Glu	Glu	Thr 525	Glu	Glu	Glu	
						ctg Leu 535										1632
						cac His										1680
						gag Glu										1728
						ccc Pro										1776
	_		_	_		cag Gln	_				_	_				1824
_			_		_	gcc Ala 615										1872
						cag Gln										1920
						ccc Pro										1968
						ctg Leu										2016
						gcc Ala										2064
						cgg Arg 695										2112
						cta Leu										2160
						ccc Pro										2208
						gcc Ala										2256
						gac Asp										2304

755		760	765	
		l Gly Cys Val	gta gag ctg gtc Val Glu Leu Val 780	
			gct gtg gtc cgc Ala Val Val Arg 795	
			ggc ttt tgc tac Gly Phe Cys Tyr	
			cag agg ttg agc Gln Arg Leu Ser 830	
	Ile Val Asp Tr		cat gga aac ggg His Gly Asn Gly 845	
cag gct ttc Gln Ala Phe 850	tac agc gac cc Tyr Ser Asp Pro 85	Ser Val Leu	tac atg tcc ctc Tyr Met Ser Leu 860	ctt cgc 2592 Leu Arg
			ggg gct cct gat Gly Ala Pro Asp 875	
			aac atg gct ttc Asn Met Ala Phe	
			tac ttg gcg gcc Tyr Leu Ala Ala 910	
			gcc ccg gat gtg Ala Pro Asp Val 925	
gtg tca tca Val Ser Ser 930	ggc ttc gat gcc Gly Phe Asp Ala 93!	Val Glu Gly	cac ccc acc cct His Pro Thr Pro 940	ctt ggg 2832 Leu Gly
			tac ctg acg aag Tyr Leu Thr Lys 955	
			gcc ctc gag gga Ala Leu Glu Gly	
-			gca tgt gtt tct Ala Cys Val Ser 990	5
			aag gtt tta cag Lys Val Leu Gln 1005	

ccc aat gca Pro Asn Ala 1010			Ser Met						3072
agc aag tac Ser Lys Tyr 1025					Ser Thr				3120
tct ctg atc Ser Leu Ile		Gln Thr						Val	3168
acc gcc atg Thr Ala Met				Val Lys			Lys		3216
cca gat gag Pro Asp Glu 107	Glu Pro								3255
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(HDAC4)	nant nega	ative mu	tant (H8	63L) of 3	human hi	stone	dea	cetylase	e - 4
gene									
gene									
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<pre><400> 6 Met Ser Ser 1 Val Glu Leu Asp Val Ala</pre>	Gln Ser 5 Leu Asn 20 Thr Ala Arg Leu Glu Gln	Pro Ala Leu Pro Asp His 55 Gln Leu 70	Arg Val 25 Leu Gln 40 Gln Phe	10 Asn His Val Ala Ser Leu Glu Leu 75	Met Pro Pro Ser 45 Pro Val 60 Leu Ala	Ser 30 Ala Ala Leu Gln	15 Thr Val Glu Lys	Val Pro Pro Gln 80	
<pre><400> 6 Met Ser Ser 1 Val Glu Leu Asp Val Ala 35 Met Asp Leu 50 Ala Leu Arg 65</pre>	Gln Ser 5 Leu Asn 20 Thr Ala Arg Leu Glu Gln Ile Gln 85	Pro Ala Leu Pro Asp His 55 Gln Leu 70 Arg Gln	Arg Val 25 Leu Gln 40 Gln Phe Gln Gln	Asn His Val Ala Ser Leu Glu Leu 75 Ile Ala 90	Met Pro Pro Ser 45 Pro Val 60 Leu Ala Glu Phe	Ser 30 Ala Ala Leu Gln	Thr Val Glu Lys Arg	Val Pro Pro Gln 80 Gln	
<pre><400> 6 Met Ser Ser 1 Val Glu Leu Asp Val Ala 35 Met Asp Leu 50 Ala Leu Arg 65 Lys Gln Gln</pre>	Gln Ser 5 Leu Asn 20 Thr Ala Arg Leu Glu Gln Ile Gln 85 Leu Ser 100 Gln Glu	Pro Ala Leu Pro Asp His 55 Gln Leu 70 Arg Gln Arg Gln	Arg Val 25 Leu Gln 40 Gln Phe Gln Gln Ile Leu His Glu 105	Asn His Val Ala Ser Leu 75 Ile Ala 90 Ala Gln	Met Pro Pro Ser 45 Pro Val 60 Leu Ala Glu Phe Leu His	Ser 30 Ala Ala Leu Gln Glu 110	Thr Val Glu Lys Arg 95	Val Pro Pro Gln 80 Gln Ile	

Lys Gln His Arg Glu Gln Lys Leu Gln Gln Leu Lys Asn Lys Glu Lys Gly Lys Glu Ser Ala Val Ala Ser Thr Glu Val Lys Met Lys Leu Gln Glu Phe Val Leu Asn Lys Lys Lys Ala Leu Ala His Arg Asn Leu Asn 185 His Cys Ile Ser Ser Asp Pro Arg Tyr Trp Tyr Gly Lys Thr Gln His Ser Ser Leu Asp Gln Ser Ser Pro Pro Gln Ser Gly Val Ser Thr Ser 215 Tyr Asn His Pro Val Leu Gly Met Tyr Asp Ala Lys Asp Asp Phe Pro 230 235 Leu Arg Lys Thr Ala Ser Glu Pro Asn Leu Lys Leu Arg Ser Arg Leu 245 250 Lys Gln Lys Val Ala Glu Arg Arg Ser Ser Pro Leu Leu Arg Arg Lys 265 Asp Gly Pro Val Val Thr Ala Leu Lys Lys Arg Pro Leu Asp Val Thr 280 275 Asp Ser Ala Cys Ser Ser Ala Pro Gly Ser Gly Pro Ser Ser Pro Asn 295 300 Asn Ser Ser Gly Ser Val Ser Ala Glu Asn Gly Ile Ala Pro Ala Val 310 315 Pro Ser Ile Pro Ala Glu Thr Ser Leu Ala His Arg Leu Val Ala Arg 325 330 Glu Gly Ser Ala Ala Pro Leu Pro Leu Tyr Thr Ser Pro Ser Leu Pro 340 345 Asn Ile Thr Leu Gly Leu Pro Ala Thr Gly Pro Ser Ala Gly Thr Ala 360 Gly Gln Gln Asp Thr Glu Arg Leu Thr Leu Pro Ala Leu Gln Gln Arg Leu Ser Leu Phe Pro Gly Thr His Leu Thr Pro Tyr Leu Ser Thr Ser Pro Leu Glu Arg Asp Gly Gly Ala Ala His Ser Pro Leu Leu Gln His Met Val Leu Glu Gln Pro Pro Ala Gln Ala Pro Leu Val Thr Gly 425 Leu Gly Ala Leu Pro Leu His Ala Gln Ser Leu Val Gly Ala Asp Arg 435 Val Ser Pro Ser Ile His Lys Leu Arg Gln His Arg Pro Leu Gly Arg Thr Gln Ser Ala Pro Leu Pro Gln Asn Ala Gln Ala Leu Gln His Leu

465					470					475					480
Val	Ile	Gln	Gln	Gln 485	His	Gln	Gln	Phe	Leu 490	Glu	Lys	His	Lys	Gln 495	Gln
Phe	Gln	Gln	Gln 500	Gln	Leu	Gln	Met	Asn 505	Lys	Ile	Ile	Pro	Lys 510	Pro	Ser
Glu	Pro	Ala 515	Arg	Gln	Pro	Glu	Ser 520	His	Pro	Glu	Glu	Thr 525	Glu	Glu	Glu
Leu	Arg 530	Glu	His	Gln	Ala	Leu 535	Leu	Asp	Glu	Pro	Tyr 540	Leu	Asp	Arg	Leu
Pro 545	Gly	Gln	Lys	Glu	Ala 550	His	Ala	Gln	Ala	Gly 555	Val	Gln	Val	Lys	Gln 560
Glu	Pro	Ile	Glu	Ser 565	Asp	Glu	Glu	Glu	Ala 570	Glu	Pro	Pro	Arg	Glu 575	Val
Glu	Pro	Gly	Gln 580	Arg	Gln	Pro	Ser	Glu 585	Gln	Glu	Leu	Leu	Phe 590	Arg	Gln
Gln	Ala	Leu 595	Leu	Leu	Glu	Gln	Gln 600	Arg	Ile	His	Gln	Leu 605	Arg	Asn	Tyr
Gln	Ala 610	Ser	Met	Glu	Ala	Ala 615	Gly	Ile	Pro	Val	Ser 620	Phe	Gly	Gly	His
Arg 625	Pro	Leu	Ser	Arg	Ala 630	Gln	Ser	Ser	Pro	Ala 635	Ser	Ala	Thr	Phe	Pro 640
Val	Ser	Val	Gln	Glu 645	Pro	Pro	Thr	Lys	Pro 650	Arg	Phe	Thr	Thr	Gly 655	Leu
Val	Tyr	Asp	Thr 660	Leu	Met	Leu	Lys	His 665	Gln	Cys	Thr	Cys	Gly 670	Ser	Ser
Ser	Ser	His 675	Pro	Glu	His	Ala	Gly 680	Arg	Ile	Gln	Ser	Ile 685	Trp	Ser	Arg
Leu	Gln 690	Glu	Thr	Gly	Leu	Arg 695	Gly	Lys	Cys	Glu	Cys 700	Ile	Arg	Gly	Arg
Lys 705	Ala	Thr	Leu	Glu	Glu 710	Leu	Gln	Thr	Val	His 715	Ser	Glu	Ala	His	Thr 720
Leu	Leu	Tyr	Gly	Thr 725	Asn	Pro	Leu	Asn	Arg 730	Gln	Lys	Leu	Asp	Ser 735	Lys
Lys	Leu	Leu	Gly 740	Ser	Leu	Ala	Ser	Val 745	Phe	Val	Arg	Leu	Pro 750	Cys	Gly
Gly	Val	Gly 755	Val	Asp	Ser	Asp	Thr 760	Ile	Trp	Asn	Glu	Val 765	His	Ser	Ala
Gly	Ala 770	Ala	Arg	Leu	Ala	Val 775	Gly	Ċys	Val	Val	Glu 780	Leu	Val	Phe	Lys
Val 785	Ala	Thr	Gly	Glu	Leu 790	Lys	Asn	Gly	Phe	Ala 795	Val	Val	Arg	Pro	Pro 800

Gly His His Ala Glu Glu Ser Thr Pro Met Gly Phe Cys Tyr Phe Asn 805 810 815

Ser Val Ala Val Ala Ala Lys Leu Leu Gln Gln Arg Leu Ser Val Ser 820 825 830

Lys Ile Leu Ile Val Asp Trp Asp Val His His Gly Asn Gly Thr Gln 835 840 845

Gln Ala Phe Tyr Ser Asp Pro Ser Val Leu Tyr Met Ser Leu Leu Arg 850 855 860

Tyr Asp Asp Gly Asn Phe Phe Pro Gly Ser Gly Ala Pro Asp Glu Val 865 870 875 880

Gly Thr Gly Pro Gly Val Gly Phe Asn Val Asn Met Ala Phe Thr Gly 885 890 895

Gly Leu Asp Pro Pro Met Gly Asp Ala Glu Tyr Leu Ala Ala Phe Arg 900 905 910

Thr Val Val Met Pro Ile Ala Ser Glu Phe Ala Pro Asp Val Val Leu 915 920 925

Val Ser Ser Gly Phe Asp Ala Val Glu Gly His Pro Thr Pro Leu Gly 930 935 940

Gly Tyr Asn Leu Ser Ala Arg Cys Phe Gly Tyr Leu Thr Lys Gln Leu 945 950 955 960

Met Gly Leu Ala Gly Gly Arg Ile Val Leu Ala Leu Glu Gly Gly His
965 970 975

Asp Leu Thr Ala Ile Cys Asp Ala Ser Glu Ala Cys Val Ser Ala Leu 980 985 990

Leu Gly Asn Glu Leu Asp Pro Leu Pro Glu Lys Val Leu Gln Gln Arg
995 1000 1005

Pro Asn Ala Asn Ala Val Arg Ser Met Glu Lys Val Met Glu Ile His 1010 1015 1020

Ser Lys Tyr Trp Arg Cys Leu Gln Arg Thr Thr Ser Thr Ala Gly Arg 1025 1030 1035 1040

Ser Leu Ile Glu Ala Gln Thr Cys Glu Asn Glu Glu Ala Glu Thr Val 1045 1050 1055

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Pro Asp Glu Glu Pro Met Glu Glu Glu Pro Pro Leu
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gac gtg tct gat gtt ggc cta ggg aag gga cgg tac tac agt gta aat Asp Val Ser Asp Val Gly Leu Gly Lys Gly Arg Tyr Tyr Ser Val Asn 215 220 225	726
gtg ccc att cag gat ggc ata caa gat gaa aaa tat tac cag atc tgt Val Pro Ile Gln Asp Gly Ile Gln Asp Glu Lys Tyr Tyr Gln Ile Cys 230 235 240	774
gaa agt gta cta aag gaa gta tac caa gcc ttt aat ccc aaa gca gtg Glu Ser Val Leu Lys Glu Val Tyr Gln Ala Phe Asn Pro Lys Ala Val 245 250 255 260	822
gtc tta cag ctg gga gct gac aca ata gct ggg gat ccc atg tgc tcc Val Leu Gln Leu Gly Ala Asp Thr Ile Ala Gly Asp Pro Met Cys Ser 265 270 275	870
ttt aac atg act cca gtg gga att ggc aag tgt ctt aag tac atc ctt Phe Asn Met Thr Pro Val Gly Ile Gly Lys Cys Leu Lys Tyr Ile Leu 280 285 290	918
caa tgg cag ttg gca aca ctc att ttg gga gga gga ggc tat aac ctt Gln Trp Gln Leu Ala Thr Leu Ile Leu Gly Gly Gly Gly Tyr Asn Leu 295 300 305	966
gcc aac acg gct cga tgc tgg aca tac ttg acc ggg gtc atc cta ggg Ala Asn Thr Ala Arg Cys Trp Thr Tyr Leu Thr Gly Val Ile Leu Gly 310 315 320	1014
aaa aca cta tcc tct gag atc cca gat cat gag ttt ttc aca gca tat Lys Thr Leu Ser Ser Glu Ile Pro Asp His Glu Phe Phe Thr Ala Tyr 325 330 335 340	1062
ggt cct gat tat gtg ctg gaa atc acg cca agc tgc cgg cca gac cgc Gly Pro Asp Tyr Val Leu Glu Ile Thr Pro Ser Cys Arg Pro Asp Arg 345 350 355	1110
aat gag ccc cac cga atc caa caa atc ctc aac tac atc aaa ggg aat Asn Glu Pro His Arg Ile Gln Gln Ile Leu Asn Tyr Ile Lys Gly Asn 360 365 370	1158
ctg aag cat gtg gtc tag ttgacagaaa gagatcaggt ttccagagct Leu Lys His Val Val 375	1206
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- <213> Homo sapiens

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Val Tyr Ile Tyr Ser Pro Glu Tyr Val Ser Met Cys Asp Ser Leu Ala 20 25

Lys Ile Pro Lys Arg Ala Ser Met Val His Ser Leu Ile Glu Ala Tyr 40

Ala Leu His Lys Gln Met Arg Ile Val Lys Pro Lys Val Ala Ser Met

Glu Glu Met Ala Thr Phe His Thr Asp Ala Tyr Leu Gln His Leu Gln 70

Lys Val Ser Gln Glu Gly Asp Asp His Pro Asp Ser Ile Glu Tyr 90

Gly Leu Gly Tyr Asp Cys Pro Ala Thr Glu Gly Ile Phe Asp Tyr Ala 100 105

Ala Ala Ile Gly Gly Ala Thr Ile Thr Ala Ala Gln Cys Leu Ile Asp 120

Gly Met Cys Lys Val Ala Ile Asn Trp Ser Gly Gly Trp His His Ala

Lys Lys Asp Glu Ala Ser Gly Phe Cys Tyr Leu Asn Asp Ala Val Leu

Gly Ile Leu Arg Leu Arg Lys Phe Glu Arg Ile Leu Tyr Val Asp

Leu Asp Leu His His Gly Asp Gly Val Glu Asp Ala Phe Ser Phe Thr

Ser Lys Val Met Thr Val Ser Leu His Lys Phe Ser Pro Gly Phe Phe 200

Pro Gly Thr Gly Asp Val Ser Asp Val Gly Leu Gly Lys Gly Arg Tyr Tyr Ser Val Asn Val Pro Ile Gln Asp Gly Ile Gln Asp Glu Lys Tyr 235 Tyr Gln Ile Cys Glu Ser Val Leu Lys Glu Val Tyr Gln Ala Phe Asn 245 250 Pro Lys Ala Val Val Leu Gln Leu Gly Ala Asp Thr Ile Ala Gly Asp 260 265 Pro Met Cys Ser Phe Asn Met Thr Pro Val Gly Ile Gly Lys Cys Leu 275 280 Lys Tyr Ile Leu Gln Trp Gln Leu Ala Thr Leu Ile Leu Gly Gly Gly 290 295 300 Gly Tyr Asn Leu Ala Asn Thr Ala Arg Cys Trp Thr Tyr Leu Thr Gly 305 310 315 320 Val Ile Leu Gly Lys Thr Leu Ser Ser Glu Ile Pro Asp His Glu Phe 325 330 Phe Thr Ala Tyr Gly Pro Asp Tyr Val Leu Glu Ile Thr Pro Ser Cys 340 345 Arg Pro Asp Arg Asn Glu Pro His Arg Ile Gln Gln Ile Leu Asn Tyr 355 Ile Lys Gly Asn Leu Lys His Val Val <210> 9 <211> 1449 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (1)..(1449) <223> human histone deacetylase-1 (HDAC1) gene atg gcg cag acg cag ggc acc cgg agg aaa gtc tgt tac tac tac gac 48 Met Ala Gln Thr Gln Gly Thr Arg Arg Lys Val Cys Tyr Tyr Asp ggg gat gtt gga aat tac tat tat gga caa ggc cac cca atg aag cct 96 Gly Asp Val Gly Asn Tyr Tyr Gly Gln Gly His Pro Met Lys Pro

20	25	30

					act Thr											144
					tat Tyr											192
	_			_	gat Asp 70	-					_	_			_	240
					gag Glu											288
					gta Val								_	_	_	336
					gtg Val											384
					aat Asn											432
					ttc Phe 150											480
					tat Tyr											528
				-	ggc Gly		_		_				_	_		576
gtc Val	atg Met	act Thr 195	gtg Val	tcc Ser	ttt Phe	cat His	aag Lys 200	tat Tyr	gga Gly	gag Glu	tac Tyr	ttc Phe 205	cca Pro	gga Gly	act Thr	624
	-		-	_	atc Ile		_				_			_	_	672
		_		_	gac Asp 230			_	_					_		720
	_	_	_	_	tcc Ser		_	_		_		_		_		768
					ggc Gly											816

					atc Ile											864
					cct Pro											912
					cgg Arg 310											960
_	_				aat Asn						_			_		1008
					aag Lys											1056
					tac Tyr											1104
					ccg Pro											
					cct Pro 390											1200
					tcg Ser					Asp						1248
					gat Asp											1296
					aaa Lys											1344
					gag Glu											1392
acc Thr 465	aag Lys	gag Glu	gag Glu	aag Lys	cca Pro 470	gaa Glu	gcc Ala	aaa Lys	GJA aaa	gtc Val 475	aag Lys	gag Glu	gag Glu	gtc Val	aag Lys 480	1440
_	gcc Ala	tga														1449

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Gly Asp Val Gly Asn Tyr Tyr Tyr Gly Gln Gly His Pro Met Lys Pro 20 25 30

His Arg Ile Arg Met Thr His Asn Leu Leu Leu Asn Tyr Gly Leu Tyr 35 40 45

Arg Lys Met Glu Ile Tyr Arg Pro His Lys Ala Asn Ala Glu Glu Met 50 55 60

Thr Lys Tyr His Ser Asp Asp Tyr Ile Lys Phe Leu Arg Ser Ile Arg 65 70 75 80

Pro Asp Asn Met Ser Glu Tyr Ser Lys Gln Met Gln Arg Phe Asn Val 85 90 95

Gly Glu Asp Cys Pro Val Phe Asp Gly Leu Phe Glu Phe Cys Gln Leu 100 105 110

Ser Thr Gly Gly Ser Val Ala Ser Ala Val Lys Leu Asn Lys Gln Gln 115 120 125

Thr Asp Ile Ala Val Asn Trp Ala Gly Gly Leu His His Ala Lys Lys 130 135 140

Ser Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp Ile Val Leu Ala Ile 145 150 155 160

Leu Glu Leu Leu Lys Tyr His Gln Arg Val Leu Tyr Ile Asp Ile Asp 165 170 175

Ile His His Gly Asp Gly Val Glu Glu Ala Phe Tyr Thr Thr Asp Arg
180 _ 185 190

Val Met Thr Val Ser Phe His Lys Tyr Gly Glu Tyr Phe Pro Gly Thr 195 200 205

Gly Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly Lys Tyr Tyr Ala Val 210 215 220

Asn Tyr Pro Leu Arg Asp Gly Ile Asp Asp Glu Ser Tyr Glu Ala Ile 225 230 235 240 Phe Lys Pro Val Met Ser Lys Val Met Glu Met Phe Gln Pro Ser Ala Val Val Leu Gln Cys Gly Ser Asp Ser Leu Ser Gly Asp Arg Leu Gly Cys Phe Asn Leu Thr Ile Lys Gly His Ala Lys Cys Val Glu Phe Val Lys Ser Phe Asn Leu Pro Met Leu Met Leu Gly Gly Gly Tyr Thr Ile Arg Asn Val Ala Arg Cys Arg Thr Tyr Glu Thr Ala Val Ala Leu Asp Thr Glu Ile Pro Asn Glu Leu Pro Tyr Asn Asp Tyr Phe Glu Tyr Phe Gly Pro Asp Phe Lys Leu His Ile Ser Pro Ser Asn Met Thr Asn Gln Asn Thr Asn Glu Tyr Leu Glu Lys Ile Lys Gln Arg Leu Phe Glu Asn Leu Arg Met Leu Pro His Ala Pro Gly Val Gln Met Gln Ala Ile Pro Glu Asp Ala Ile Pro Glu Glu Ser Gly Asp Glu Asp Glu Asp Asp Pro Asp Lys Arg Ile Ser Ile Cys Ser Ser Asp Lys Arg Ile Ala Cys Glu Glu Glu Phe Ser Asp Ser Glu Glu Glu Gly Gly Gly Arg Lys Asn Ser Ser Asn Phe Lys Lys Ala Lys Arg Val Lys Thr Glu Asp Glu Lys Glu Lys Asp Pro Glu Glu Lys Lys Glu Val Thr Glu Glu Lys Thr Lys Glu Glu Lys Pro Glu Ala Lys Gly Val Lys Glu Glu Val Lys

Leu Ala

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cac cga atc cgc at His Arg Ile Arg Me 35	=			144
cga aaa atg gaa at Arg Lys Met Glu Il 50			n Ala Glu Glu Met	192
acc aag tac cac ag Thr Lys Tyr His Se 65				240
cca gat aac atg tc Pro Asp Asn Met Se 85				288
ggt gag gac tgt cc Gly Glu Asp Cys Pr 100				336
tct act ggt ggt tc Ser Thr Gly Gly Se 115				384
acg gac atc gct gt Thr Asp Ile Ala Va 130			s Leu Ala Lys Lys	432
tcc gag gca tct gg Ser Glu Ala Ser Gl 145				480
ctg gaa ctg cta aa Leu Glu Leu Leu Ly 16	s Tyr His Gln			528

								gag Glu 185								576
								tat Tyr								624
								ggc Gly								672
		_		_	_			gat Asp	_					_		720
	_	_	_	_			_	atg Met		_		_		_		768
								tcc Ser 265								816
								cac His								864
								atg Met								912
								aca Thr								960
_	_							cca Pro			_			_		1008
								atc Ile 345								1056
_		_				_		aag Lys			_	_	_			1104
								cct Pro								1152
								agt Ser								1200
								tcc Ser								1248
gag	gaa	gag	ttc	tcc	gat	tct	gaa	gag	gag	gga	gag	aaa	ggc	cgc	aag	1296

	•															
Glu	Glu	Glu	Phe 420	Ser	Asp	Ser	Glu	Glu 425	Glu	Gly	Glu	Gly	Gly 430	Arg	Lys	
														gat Asp		1344
														gag Glu		1392
														gtc Val		1440
_	gcc Ala	_														1449
<211 <212	0 >	182	Eicia	al Se	equer	nce										
<220 <223	3 > I				ative	e mut	ant	(H1	40K,	H14:	lL) (of hu	ıman	hist	cone	deacetyla
	3> I	Domin (HDAC			ative	e mut	cant	(H14	40K,	H14:	lL) (of hu	ıman	hist	cone	deacetyla
<223	3 > I 0 > 1	(HDA0	C1) g	gene										hist Tyr 15		deacetyla
<223 <400 Met 1	3> I 0> 1 Ala	(HDAC 12 Gln	C1) o	gene Gln 5	Gly	Thr	Arg	Arg	Lys 10	Val	Cys	Tyr	Tyr	Tyr	Asp	deacetyla
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<223 <400 Met 1 Gly His	3> I 0> 3 Ala Asp Arg Lys 50	(HDAG 12 Gln Val Ile 35 Met	Thr Gly 20 Arg	Gln 5 Asn Met	Gly Tyr Thr	Thr Tyr His Arg	Arg Tyr Asn 40	Arg Gly 25 Leu	Lys 10 Gln Leu	Val Gly Leu Ala	Cys His Asn Asn 60	Tyr Pro Tyr 45	Tyr Met 30 Gly	Tyr 15 Lys Leu	Asp Pro Tyr Met	deacetyla
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<223 <400 Met 1 Gly His Arg Thr 65	Asp Arg Lys Lys Asp	(HDAC) 12 Gln Val Ile 35 Met Tyr	Thr Gly 20 Arg Glu His	Gln 5 Asn Met Ile Ser 85	Gly Tyr Thr Tyr Asp 70 Glu	Thr Tyr His Arg 55 Asp	Arg Tyr Asn 40 Pro Tyr	Arg Gly 25 Leu His	Lys 10 Gln Leu Lys Gln 90	Val Gly Leu Ala Phe 75	Cys His Asn 60 Leu Gln	Tyr Pro Tyr 45 Ala Arg	Tyr Met 30 Gly Glu Ser	Tyr 15 Lys Leu Glu Ile	Asp Pro Tyr Met Arg 80	deacetyla

Thr Asp Ile Ala Val Asn Trp Ala Gly Gly Leu Lys Leu Ala Lys Lys 130 135 Ser Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp Ile Val Leu Ala Ile Leu Glu Leu Leu Lys Tyr His Gln Arg Val Leu Tyr Ile Asp Ile Asp Ile His His Gly Asp Gly Val Glu Glu Ala Phe Tyr Thr Thr Asp Arg 185 Val Met Thr Val Ser Phe His Lys Tyr Gly Glu Tyr Phe Pro Gly Thr 200 Gly Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly Lys Tyr Tyr Ala Val 215 Asn Tyr Pro Leu Arg Asp Gly Ile Asp Asp Glu Ser Tyr Glu Ala Ile 230 235 Phe Lys Pro Val Met Ser Lys Val Met Glu Met Phe Gln Pro Ser Ala 245 250 Val Val Leu Gln Cys Gly Ser Asp Ser Leu Ser Gly Asp Arg Leu Gly 260 265 Cys Phe Asn Leu Thr Ile Lys Gly His Ala Lys Cys Val Glu Phe Val 280 Lys Ser Phe Asn Leu Pro Met Leu Met Leu Gly Gly Gly Tyr Thr Ile Arg Asn Val Ala Arg Cys Arg Thr Tyr Glu Thr Ala Val Ala Leu Asp Thr Glu Ile Pro Asn Glu Leu Pro Tyr Asn Asp Tyr Phe Glu Tyr 330 Phe Gly Pro Asp Phe Lys Leu His Ile Ser Pro Ser Asn Met Thr Asn 345 Gln Asn Thr Asn Glu Tyr Leu Glu Lys Ile Lys Gln Arg Leu Phe Glu

Asn Leu Arg Met Leu Pro His Ala Pro Gly Val Gln Met Gln Ala Ile 375 Pro Glu Asp Ala Ile Pro Glu Glu Ser Gly Asp Glu Asp Glu Asp Asp 395 Pro Asp Lys Arg Ile Ser Ile Cys Ser Ser Asp Lys Arg Ile Ala Cys 405 410 Glu Glu Glu Phe Ser Asp Ser Glu Glu Glu Gly Gly Gly Arg Lys 420 425 Asn Ser Ser Asn Phe Lys Lys Ala Lys Arg Val Lys Thr Glu Asp Glu 435 440 445 Lys Glu Lys Asp Pro Glu Glu Lys Lys Glu Val Thr Glu Glu Glu Lys 450 455 460 Thr Lys Glu Glu Lys Pro Glu Ala Lys Gly Val Lys Glu Glu Val Lys 465 470 475 480 Leu Ala <210> 13 <211> 1449 <212> DNA <213> Artificial Sequence <220> <221> CDS <222> (1)..(1449) <223> Dominant negative mutant (H199L) of human histone deacetylase-1 (HDAC1) gene <400> 13 atg gcg cag acg cag ggc acc cgg agg aaa gtc tgt tac tac tac gac 48 Met Ala Gln Thr Gln Gly Thr Arg Arg Lys Val Cys Tyr Tyr Tyr Asp ggg gat gtt gga aat tac tat tat gga caa ggc cac cca atg aag cct 96 Gly Asp Val Gly Asn Tyr Tyr Gly Gln Gly His Pro Met Lys Pro 20 cac cga atc cgc atg act cat aat ttg ctg ctc aac tat ggt ctc tac 144 His Arg Ile Arg Met Thr His Asn Leu Leu Asn Tyr Gly Leu Tyr 35 cga aaa atg gaa atc tat cgc cct cac aaa gcc aat gct gag gag atg 192 Arg Lys Met Glu Ile Tyr Arg Pro His Lys Ala Asn Ala Glu Glu Met

	_			_	_	_					_	_	tcc Ser		_	240
													ttc Phe			288
													tgt Cys 110			336
													aag Lys			384
													gca Ala			432
													ttg Leu			480
													gac Asp			528
													acg Thr 190			576
													cca Pro			624
	_			_			_				_		tat Tyr	_	_	672
													gag Glu			720
													cct Pro			768
gtg Val	gtc Val	tta Leu	cag Gln 260	tgt Cys	ggc Gly	tca Ser	gac Asp	tcc Ser 265	cta Leu	tct Ser	GJA aaa	gat Asp	cgg Arg 270	tta Leu	ggt Gly	816
													gaa Glu			864
													ggt Gly			912
att	cgt	aac	gtt	gcc	cgg	tgc	agg	aca	tat	gag	aca	gct	gtg	gcc	ctg	960

Ile Arg Asn Va	l Ala Arg Cy 310	s Arg Thr Ty:	r Glu Thr Ala Va 315	l Ala Leu 320
			c aat gac tac tt r Asn Asp Tyr Pho O	
	Phe Lys Le	_	t cct tcc aat atg r Pro Ser Asn Med 350	Thr Asn
			c aaa cag cga cto e Lys Gln Arg Leo 365	
		s Ala Pro Gl	g gtc caa atg cag y Val Gln Met Gli 380	
			c gat gag gac gaa y Asp Glu Asp Glu 395	
			t gac aaa cga at r Asp Lys Arg Ile)	
	e Ser Asp Se		g gga gag ggg gg ı Gly Glu Gly Gly 430	y Arg Lys
			a gtc aaa aca gag g Val Lys Thr Gli 445	
		u Lys Lys Gl	a gtc acc gaa gag ı Val Thr Glu Glu 460	
	ı Lys Pro Gl		g gtc aag gag gag y Val Lys Glu Glu 475	
ttg gcc tga Leu Ala				1449
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Gly Asp Val Gly Asn Tyr Tyr Gly Gln Gly His Pro Met Lys Pro His Arg Ile Arg Met Thr His Asn Leu Leu Leu Asn Tyr Gly Leu Tyr 40 Arg Lys Met Glu Ile Tyr Arg Pro His Lys Ala Asn Ala Glu Glu Met 55 Thr Lys Tyr His Ser Asp Asp Tyr Ile Lys Phe Leu Arg Ser Ile Arg 70 75 Pro Asp Asn Met Ser Glu Tyr Ser Lys Gln Met Gln Arg Phe Asn Val 90 Gly Glu Asp Cys Pro Val Phe Asp Gly Leu Phe Glu Phe Cys Gln Leu 100 105 110 Ser Thr Gly Gly Ser Val Ala Ser Ala Val Lys Leu Asn Lys Gln Gln 115 120 Thr Asp Ile Ala Val Asn Trp Ala Gly Gly Leu His His Ala Lys Lys 130 135 Ser Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp Ile Val Leu Ala Ile 145 Leu Glu Leu Lys Tyr His Gln Arg Val Leu Tyr Ile Asp Ile Asp Ile His His Gly Asp Gly Val Glu Glu Ala Phe Tyr Thr Thr Asp Arg 180 Val Met Thr Val Ser Phe Leu Lys Tyr Gly Glu Tyr Phe Pro Gly Thr 195 Gly Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly Lys Tyr Tyr Ala Val 210 Asn Tyr Pro Leu Arg Asp Gly Ile Asp Asp Glu Ser Tyr Glu Ala Ile 225 Phe Lys Pro Val Met Ser Lys Val Met Glu Met Phe Gln Pro Ser Ala 245 250

Val Val Leu Gln Cys Gly Ser Asp Ser Leu Ser Gly Asp Arg Leu Gly Cys Phe Asn Leu Thr Ile Lys Gly His Ala Lys Cys Val Glu Phe Val Ser Phe Asn Leu Pro Met Leu Met Leu Gly Gly Gly Gly Tyr Thr 290 Arg Asn Val Ala Arg Cys Arg Thr Tyr Glu Thr Ala Val Ala Leu 320

Asp Thr Glu Ile Pro Asn Glu Leu Pro Tyr Asn Asp Tyr Phe Glu Tyr 325 330 335

Phe Gly Pro Asp Phe Lys Leu His Ile Ser Pro Ser Asn Met Thr Asn 340 345 350

Gln Asn Thr Asn Glu Tyr Leu Glu Lys Ile Lys Gln Arg Leu Phe Glu 355 360 365

Asn Leu Arg Met Leu Pro His Ala Pro Gly Val Gln Met Gln Ala Ile 370 375 380

Pro Glu Asp Ala Ile Pro Glu Glu Ser Gly Asp Glu Asp Glu Asp Asp 385 390 395 400

Pro Asp Lys Arg Ile Ser Ile Cys Ser Ser Asp Lys Arg Ile Ala Cys 405 410 415

Glu Glu Glu Phe Ser Asp Ser Glu Glu Glu Gly Glu Gly Arg Lys 420 425 430

Asn Ser Ser Asn Phe Lys Lys Ala Lys Arg Val Lys Thr Glu Asp Glu 435 440 445

Lys Glu Lys Asp Pro Glu Glu Lys Lys Glu Val Thr Glu Glu Glu Lys 450 455 460

Thr Lys Glu Glu Lys Pro Glu Ala Lys Gly Val Lys Glu Glu Val Lys 465 470 475 480

Leu Ala

<	210 211 212 213	L> 2> :	15 1287 DNA Homo	sap:	iens												
<	220 221 222 223	L> 2>	CDS (1). humaı	-		e dea	acety	ylas	e-3	(HDA	C3) (gene					
а	let	gcc	15 aag Lys														48
			gga Gly														96
H	at	agc Ser	ctg Leu 35	gtc Val	ctg Leu	cat His	tac Tyr	ggt Gly 40	ctc Leu	tat Tyr	aag Lys	aag Lys	atg Met 45	atc Ile	gtc Val	ttc Phe	144
	_		tac Tyr						_	_	_	_					192
A			att Ile														240
F	tc he	acc Thr	aag Lys	agt Ser	ctt Leu 85	aat Asn	gcc Ala	ttc Phe	aac Asn	gta Val 90	ggc Gly	gat Asp	gac Asp	tgc Cys	cca Pro 95	gtg Val	288
			Gl ^A aaa														336
			gca Ala 115	Thr	Gln	Leu	Asn		Lys	Ile	Cys	Asp	Ile	Ala			384
			ggt Gly														432
С	gc ys 45	tat Tyr	gtc Val	aac Asn	gac Asp	att Ile 150	gtg Val	att Ile	ggc Gly	atc Ile	ctg Leu 155	gag Glu	ctg Leu	ctc Leu	aag Lys	tac Tyr 160	480
			cgg Arg														528
			gaa Glu														576
			tac Tyr														624

195	:	200	205	
	gag agt ggc cgc ' Glu Ser Gly Arg ' 215	-		
	gat gac cag agt ' Asp Asp Gln Ser ' 230	-		
	gtg gac ttc tac (Val Asp Phe Tyr (245			
Gly Ala Asp	tct ctg ggc tgt g Ser Leu Gly Cys 2 260		_	_
	cat ggg gaa tgc q His Gly Glu Cys			
	gtg ctg ggt ggt (Val Leu Gly Gly (295			
	aca tat gag aca f Thr Tyr Glu Thr 8 310			_
	ccc tat agt gaa : Pro Tyr Ser Glu : 325			
Thr Leu His	cca gat gtc agc a Pro Asp Val Ser 1 340			
	gac cag atc ctc o Asp Gln Ile Leu o	_		_
	gca cct agt gtc (Ala Pro Ser Val (375			
	gac agg act gat o Asp Arg Thr Asp o 390			
	tat agc agg cca o Tyr Ser Arg Pro o 405			
Asp His Asp	aat gac aag gaa a Asn Asp Lys Glu 8 420			1287

<210> 16 <211> 428

<212> PRT

<213> Homo sapiens

<400> 16

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His Tyr Gly Ala Gly His Pro Met Lys Pro His Arg Leu Ala Leu Thr 20 25 30

His Ser Leu Val Leu His Tyr Gly Leu Tyr Lys Lys Met Ile Val Phe 35 40

Lys Pro Tyr Gln Ala Ser Gln His Asp Met Cys Arg Phe His Ser Glu 50 55 60

Asp Tyr Ile Asp Phe Leu Gln Arg Val Ser Pro Thr Asn Met Gln Gly 65 70 75 80

Phe Thr Lys Ser Leu Asn Ala Phe Asn Val Gly Asp Asp Cys Pro Val 85 90 95'

Phe Pro Gly Leu Phe Glu Phe Cys Ser Arg Tyr Thr Gly Ala Ser Leu 100 105 110

Gln Gly Ala Thr Gln Leu Asn Asn Lys Ile Cys Asp Ile Ala Ile Asn 115 120 125

Trp Ala Gly Gly Leu His His Ala Lys Lys Phe Glu Ala Ser Gly Phe 130 135 140

Cys Tyr Val Asn Asp Ile Val Ile Gly Ile Leu Glu Leu Leu Lys Tyr 145 150 155 160

His Pro Arg Val Leu Tyr Ile Asp Ile Asp Ile His His Gly Asp Gly
165 170 175

Val Gln Glu Ala Phe Tyr Leu Thr Asp Arg Val Met Thr Val Ser Phe 180 185 190

His Lys Tyr Gly Asn Tyr Phe Phe Pro Gly Thr Gly Asp Met Tyr Glu 195 200 205

Val Gly Ala Glu Ser Gly Arg Tyr Tyr Cys Leu Asn Val Pro Leu Arg 210 215 220

Asp Gly Ile Asp Asp Gln Ser Tyr Lys His Leu Phe Gln Pro Val Ile

225	230	235	240
223	230	2,7,7	2.40

Asn Gln Val Val Asp Phe Tyr Gln Pro Thr Cys Ile Val Leu Gln Cys

Gly Ala Asp Ser Leu Gly Cys Asp Arg Leu Gly Cys Phe Asn Leu Ser 265

Ile Arg Gly His Gly Glu Cys Val Glu Tyr Val Lys Ser Phe Asn Ile 280

Pro Leu Leu Val Leu Gly Gly Gly Tyr Thr Val Arg Asn Val Ala 295

Arg Cys Trp Thr Tyr Glu Thr Ser Leu Leu Val Glu Glu Ala Ile Ser 310 315

Glu Glu Leu Pro Tyr Ser Glu Tyr Phe Glu Tyr Phe Ala Pro Asp Phe 325 330

Thr Leu His Pro Asp Val Ser Thr Arg Ile Glu Asn Gln Asn Ser Arg 340 345

Gln Tyr Leu Asp Gln Ile Leu Gln Thr Ile Phe Glu Asn Leu Lys Met 360

Leu Asn His Ala Pro Ser Val Gln Ile His Asp Val Pro Ala Asp Leu 375

Leu Thr Tyr Asp Arg Thr Asp Glu Ala Asp Ala Glu Glu Arg Gly Pro 390

Glu Glu Asn Tyr Ser Arg Pro Glu Ala Pro Asn Glu Phe Tyr Asp Gly

Asp His Asp Asn Asp Lys Glu Ser Asp Val Glu Ile 420

<210> 17 <211> 1287 <212> DNA <213> Artificial Sequence

<220>

<221> CDS <222> (1)..(1287)

<223> Dominant negative mutant (H134K, H135L) of human histone deacetylase-3 (HDAC3) gene

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cac tac gga His Tyr Gly			_		_	96
cat agc ctg His Ser Leu 35	-		_		_	144
aag cca tac Lys Pro Tyr 50						192
gac tac att of Asp Tyr Ile 2			_			240
ttc acc aag						288
ttt ccc ggg			r Arg Tyr		a Ser Leu	336
caa gga gca Gln Gly Ala 115				-		384
tgg gct ggt g Trp Ala Gly 0			-			432
tgc tat gtc a Cys Tyr Val 2 145						- 480
cac cct cgg (528
gtt caa gaa (Val Gln Glu			p Arg Val		Ser Phe	576
cac aaa tac q His Lys Tyr (195					_	624
gtc ggg gca (Val Gly Ala (210						672
gat ggc att g Asp Gly Ile 2 225		_	_		_	720

	_	_		_		tac Tyr			_	_				_	_	768
						tgt Cys										816
						tgc Cys										864
						ggt Gly 295					_	_		_	_	912
						aca Thr										960
						gaa Glu										1008
						agc Ser										1056
						ctc Leu										1104
						gtc Val 375										1152
						gat Asp										1200
						cca Pro										1248
						gaa Glu						taa				1287
<210 <211 <212 <213	.> 4 !> 1	18 128 PRT Artif	Ficia	al Se	equer	nce										
<220 <223	3 > I	Domir (HDAC	nant C3) <u>c</u>	nega jene	ative	e mut	ant	(н13	4K,	Н135	SL) c	of hu	ıman	hist	one	deacetylase-3
<400)> 1	18														

Met Ala Lys Thr Val Ala Tyr Phe Tyr Asp Pro Asp Val Gly Asn Phe

His Tyr Gly Ala Gly His Pro Met Lys Pro His Arg Leu Ala Leu Thr 20 25 30

His Ser Leu Val Leu His Tyr Gly Leu Tyr Lys Lys Met Ile Val Phe 35 40 45

Lys Pro Tyr Gln Ala Ser Gln His Asp Met Cys Arg Phe His Ser Glu 50 55 60

Asp Tyr Ile Asp Phe Leu Gln Arg Val Ser Pro Thr Asn Met Gln Gly 65 70 75 80

Phe Thr Lys Ser Leu Asn Ala Phe Asn Val Gly Asp Asp Cys Pro Val 85 90 95

Phe Pro Gly Leu Phe Glu Phe Cys Ser Arg Tyr Thr Gly Ala Ser Leu 100 105 110

Gln Gly Ala Thr Gln Leu Asn Asn Lys Ile Cys Asp Ile Ala Ile Asn 115 120 125

Trp Ala Gly Gly Leu Lys Leu Ala Lys Lys Phe Glu Ala Ser Gly Phe 130 135 140

Cys Tyr Val Asn Asp Ile Val Ile Gly Ile Leu Glu Leu Leu Lys Tyr 145 150 155 160

His Pro Arg Val Leu Tyr Ile Asp Ile Asp Ile His His Gly Asp Gly 165 170 175

Val Gln Glu Ala Phe Tyr Leu Thr Asp Arg Val Met Thr Val Ser Phe 180 185 190

His Lys Tyr Gly Asn Tyr Phe Phe Pro Gly Thr Gly Asp Met Tyr Glu 195 200 205

Val Gly Ala Glu Ser Gly Arg Tyr Tyr Cys Leu Asn Val Pro Leu Arg 210 215 220

Asp Gly Ile Asp Asp Gln Ser Tyr Lys His Leu Phe Gln Pro Val Ile 225 230 235 240

Asn Gln Val Val Asp Phe Tyr Gln Pro Thr Cys Ile Val Leu Gln Cys 245 250 255

Gly Ala Asp Ser Leu Gly Cys Asp Arg Leu Gly Cys Phe Asn Leu Ser Ile Arg Gly His Gly Glu Cys Val Glu Tyr Val Lys Ser Phe Asn Ile 280 Pro Leu Leu Val Leu Gly Gly Gly Tyr Thr Val Arg Asn Val Ala 295 300 Arg Cys Trp Thr Tyr Glu Thr Ser Leu Leu Val Glu Glu Ala Ile Ser 310 320 315 Glu Glu Leu Pro Tyr Ser Glu Tyr Phe Glu Tyr Phe Ala Pro Asp Phe 325 330 Thr Leu His Pro Asp Val Ser Thr Arg Ile Glu Asn Gln Asn Ser Arg 340 345 Gln Tyr Leu Asp Gln Ile Leu Gln Thr Ile Phe Glu Asn Leu Lys Met 355 360 Leu Asn His Ala Pro Ser Val Gln Ile His Asp Val Pro Ala Asp Leu 370 375 380 Leu Thr Tyr Asp Arg Thr Asp Glu Ala Asp Ala Glu Glu Arg Gly Pro 385 390 395 Glu Glu Asn Tyr Ser Arg Pro Glu Ala Pro Asn Glu Phe Tyr Asp Gly 405 Asp His Asp Asn Asp Lys Glu Ser Asp Val Glu Ile 420 <210> 19 <211> 1287 <212> DNA <213> Artificial Sequence

<220> <221> CDS <222> (1)..(1287)

<223> Dominant negative mutant (H193L) of human histone deacetylase-3 (HDAC3)

<400> 19

gene

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		g ccc cat cgc ctg gca s Pro His Arg Leu Ala 30	_
		c tat aag aag atg atc u Tyr Lys Lys Met Ile 45	
		c atg tgc cgc ttc cac p Met Cys Arg Phe His 60	
		c agc ccc acc aat atg l Ser Pro Thr Asn Met 75	
	<u>-</u>	c gta ggc gat gac tgc n Val Gly Asp Asp Cys 90	
		g cgt tac aca ggc gca r Arg Tyr Thr Gly Ala 5 110	_
		g atc tgt gat att gcc s Ile Cys Asp Ile Ala 125	
		g aag ttt gag gcc tct s Lys Phe Glu Ala Ser 140	
_		c atc ctg gag ctg ctc y Ile Leu Glu Leu Leu 155	_
	_	t gac atc cac cat ggt e Asp Ile His His Gly 170	3 3 3 3 3
		c cgg gtc atg acg gtg p Arg Val Met Thr Val 5 190	
		t ggc aca ggt gac atg o Gly Thr Gly Asp Met 205	_
		c tgt ctg aac gtg ccc r Cys Leu Asn Val Pro 220	3 32
		g cac ctt ttc cag ccg s His Leu Phe Gln Pro 235	_
		c acg tgc att gtg ctc o Thr Cys Ile Val Leu 250	

gga gct gac tct ctg ggc tgt gat cga ttg ggc tgc ttt aac ctc agc 8 Gly Ala Asp Ser Leu Gly Cys Asp Arg Leu Gly Cys Phe Asn Leu Ser 260 265 270	316
atc cga ggg cat ggg gaa tgc gtt gaa tat gtc aag agc ttc aat atc Ile Arg Gly His Gly Glu Cys Val Glu Tyr Val Lys Ser Phe Asn Ile 275 280 285	364
cct cta ctc gtg ctg ggt ggt ggt tat act gtc cga aat gtt gcc 9 Pro Leu Leu Val Leu Gly Gly Gly Tyr Thr Val Arg Asn Val Ala 290 295 300	912
cgc tgc tgg aca tat gag aca tcg ctg ctg gta gaa gag gcc att agt Arg Cys Trp Thr Tyr Glu Thr Ser Leu Leu Val Glu Glu Ala Ile Ser 305 310 315 320	960
gag gag ctt ccc tat agt gaa tac ttc gag tac ttt gcc cca gac ttc 10 Glu Glu Leu Pro Tyr Ser Glu Tyr Phe Glu Tyr Phe Ala Pro Asp Phe 325 330 335	800
aca ctt cat cca gat gtc agc acc cgc atc gag aat cag aac tca cgc Thr Leu His Pro Asp Val Ser Thr Arg Ile Glu Asn Gln Asn Ser Arg 340 345 350	56
cag tat ctg gac cag atc ctc cag aca atc ttt gaa aac ctg aag atg Gln Tyr Leu Asp Gln Ile Leu Gln Thr Ile Phe Glu Asn Leu Lys Met 355 360 365	L04
ctg aac cat gca cct agt gtc cag att cat gac gtg cct gca gac ctc 11 Leu Asn His Ala Pro Ser Val Gln Ile His Asp Val Pro Ala Asp Leu 370 375 380	L52
ctg acc tat gac agg act gat gag gct gat gca gag gag agg ggt cct Leu Thr Tyr Asp Arg Thr Asp Glu Ala Asp Ala Glu Glu Arg Gly Pro 385 390 395 400	200
gag gag aac tat agc agg cca gag gca ccc aat gag ttc tat gat gga 12 Glu Glu Asn Tyr Ser Arg Pro Glu Ala Pro Asn Glu Phe Tyr Asp Gly 405 410 415	248
gac cat gac aat gac aag gaa agc gat gtg gag att taa 12 Asp His Asp Asn Asp Lys Glu Ser Asp Val Glu Ile 420 425	287
<210> 20 <211> 428 <212> PRT <213> Artificial Sequence	
<220> <223> Dominant negative mutant (H193L) of human histone deacetylase-3 (HDAC3) gene	i
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His Tyr Gly Ala Gly His Pro Met Lys Pro His Arg Leu Ala Leu Thr His Ser Leu Val Leu His Tyr Gly Leu Tyr Lys Lys Met Ile Val Phe Lys Pro Tyr Gln Ala Ser Gln His Asp Met Cys Arg Phe His Ser Glu Asp Tyr Ile Asp Phe Leu Gln Arg Val Ser Pro Thr Asn Met Gln Gly Phe Thr Lys Ser Leu Asn Ala Phe Asn Val Gly Asp Asp Cys Pro Val Phe Pro Gly Leu Phe Glu Phe Cys Ser Arg Tyr Thr Gly Ala Ser Leu 100 105 Gln Gly Ala Thr Gln Leu Asn Asn Lys Ile Cys Asp Ile Ala Ile Asn 115 120 Trp Ala Gly Gly Leu His His Ala Lys Lys Phe Glu Ala Ser Gly Phe 130 135 Cys Tyr Val Asn Asp Ile Val Ile Gly Ile Leu Glu Leu Lys Tyr 145 150 His Pro Arg Val Leu Tyr Ile Asp Ile Asp Ile His His Gly Asp Gly 165 170 Val Gln Glu Ala Phe Tyr Leu Thr Asp Arg Val Met Thr Val Ser Phe 180 Leu Lys Tyr Gly Asn Tyr Phe Phe Pro Gly Thr Gly Asp Met Tyr Glu 195 Val Gly Ala Glu Ser Gly Arg Tyr Tyr Cys Leu Asn Val Pro Leu Arg 210

Asn Gln Val Val Asp Phe Tyr Gln Pro Thr Cys Ile Val Leu Gln Cys 245 250 255

Asp Gly Ile Asp Asp Gln Ser Tyr Lys His Leu Phe Gln Pro Val Ile

225

Gly Ala Asp Ser Leu Gly Cys Asp Arg Leu Gly Cys Phe Asn Leu Ser

260	265	270
200	203	2,0

Ile Arg Gly His Gly Glu Cys Val Glu Tyr Val Lys Ser Phe Asn Ile Pro Leu Leu Val Leu Gly Gly Gly Tyr Thr Val Arg Asn Val Ala Arg Cys Trp Thr Tyr Glu Thr Ser Leu Leu Val Glu Glu Ala Ile Ser 315 Glu Glu Leu Pro Tyr Ser Glu Tyr Phe Glu Tyr Phe Ala Pro Asp Phe 330 Thr Leu His Pro Asp Val Ser Thr Arg Ile Glu Asn Gln Asn Ser Arg 345 Gln Tyr Leu Asp Gln Ile Leu Gln Thr Ile Phe Glu Asn Leu Lys Met 360 Leu Asn His Ala Pro Ser Val Gln Ile His Asp Val Pro Ala Asp Leu 375 Leu Thr Tyr Asp Arg Thr Asp Glu Ala Asp Ala Glu Glu Arg Gly Pro 390 395 Glu Glu Asn Tyr Ser Arg Pro Glu Ala Pro Asn Glu Phe Tyr Asp Gly 405 410 Asp His Asp Asn Asp Lys Glu Ser Asp Val Glu Ile 420 <210> 21 <211> 1458 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (1)..(1458) <223> human N-CoR (RD3) gene <400> 21 gaa gtc ctt cag cct gct cca cat caa gtg ata act aat ctc cct gaa Glu Val Leu Gln Pro Ala Pro His Gln Val Ile Thr Asn Leu Pro Glu

10

ggc gtt cgg ctt ccg aca act cga cca acc agg cca ccg ccc cct ctc

Gly Val Arg Leu Pro Thr Thr Arg Pro Thr Arg Pro Pro Pro Leu 20 25 30 48

										cca Pro 45				•	144
					_					tat Tyr					192
		_	_				_		_	ccg Pro		_			240
										gcc Ala					288
	_			_	_	_	_			cga Arg	_				336
										gaa Glu 125					384
_			_	 _			_	 _		act Thr					432
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										ata Ile					528
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										atc Ile					720
										GJA aaa					768
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						999 Gly 295									912
_	_					ccc Pro					 _	_			960
	_	_		_		gcc Ala							_		1008
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	_				_	gaa Glu	_				_		_	_	1104
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			_			agc Ser				_	 _		_	_	1248
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Arg Glu Gly Thr Arg Ser Pro Arg Thr Ala His Glu Ile Ser Leu Lys

230

Arg Ser Tyr Glu Ser Val Glu Gly Asn Ile Lys Gln Gly Met Ser Met Arg Glu Ser Pro Val Ser Ala Pro Leu Glu Gly Leu Ile Cys Arg Ala Leu Pro Arg Gly Ser Pro His Ser Asp Leu Lys Glu Arg Thr Val Leu 280 Ser Gly Ser Ile Met Gln Gly Thr Pro Arg Ala Thr Thr Glu Ser Phe Glu Asp Gly Leu Lys Tyr Pro Lys Gln Ile Lys Arg Glu Ser Pro Pro 310 Ile Arg Ala Phe Glu Gly Ala Ile Thr Lys Gly Lys Pro Tyr Asp Gly 325 330 Ile Thr Thr Ile Lys Glu Met Gly Arg Ser Ile His Glu Ile Pro Arg 345 Gln Asp Ile Leu Thr Gln Glu Ser Arg Lys Thr Pro Glu Val Val Gln 360 Ser Thr Arg Pro Ile Ile Glu Gly Ser Ile Ser Gln Gly Thr Pro Ile 375 Lys Phe Asp Asn Asn Ser Gly Gln Ser Ala Ile Lys His Asn Val Lys 390 Ser Leu Ile Thr Gly Pro Ser Lys Leu Ser Arg Gly Met Pro Pro Leu Glu Ile Val Pro Glu Asn Ile Lys Val Val Glu Arg Gly Lys Tyr Glu Asp Val Lys Ala Gly Glu Thr Val Arg Ser Arg His Thr Ser Val Val Ser Ser Gly Pro Ser Val Leu Arg Ser Thr Leu His Glu Ala Pro Lys 455

475

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                                                                      120
tttaagtatt ctaatcttag tatttctcta gctgacatgt aagaagcaat ctatcttatt
                                                                      180
gtatgcaatt agctcattgt gtggataaaa aggtaaaacc attctgaaac aggaaaccaa
                                                                      240
tacacttcct gtttaatcaa caaatctaaa catttattct tttcatctgt ttactcttgc
                                                                      300
tcttgtccac cacaatatgc tattcacatg ttcagtgtag ttttaggaca aagaaaattt
                                                                      360
tctgagttac ttttgtatcc ccacccctt aaagaaagga ggaaaaactg tttcatacag
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aaggcgttaa ttgcatgaat tagagctatc acctaagtgt gggctaatgt aacaaagagg
                                                                      480
gatttcacct acatccattc agtcagtctt tgggggttta aagaaattcc aaagagtcat
                                                                      540
cagaagagga aaaatgaagg taatgttttt tcagacaggt aaagtctttg aaaatatgtg
                                                                      600
taatatgtaa aacattttga cacccccata atatttttcc agaattaaca gtataaattg
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Pro Val Ser Tyr Gln Asn

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                                                                      120
aaacagtacc tcaagctcaa taagcatttt aagtattcta atcttagtat ttctctagct
                                                                      180
gacatgtaag aagcaatcta tottattgta tgcaattago totttgtgtg gataaaaagg
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taaaaccatt ctgaaacagg aaaccaatac acttcctgtt taatcaacaa atctaaacat
                                                                      300
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                                                                      360
agtgtagttt tatgacaaag aaaattttct gagttacttt tgtatcccca cccccttaaa
                                                                      420
gaaaggagga aaaactgttt catacagaag gcgttaattg catgaattag agctatcacc
                                                                      480
taagtgtggg ctaatgtaac aaagagggat ttcacctaca tccattcagt cagtctttgg
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gggtttaaag aaattccaaa gagtcatcag aagaggaaaa atgaaggtaa tgttttttca
                                                                      600
gactggtaaa gtctttgaaa atatgtgtaa tatgtaaaac attttgacac ccccataata
                                                                      660
tttttccaga attaacagta taaattgcat ctcttgttca agagttccct atcactcttt
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aatcactact cacagtaacc tcaactcctg ccacaatgta caggatgcaa ctcctgt
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<210>
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<211>
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     PCR primer for amplifying the 5'-flanking region of Human interleukin-
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       (IL-2) gene
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                                                                      60
ttattetttt catetgttta etettgetet tgtecaccae aatatgetat teacatgtte
                                                                     120
agtgtagttt tatgacaaag aaaattttct gagttacttt tgtatcccca ccccttaaa
                                                                     180
gaaaggagga aaaactgttt catacagaag gcgttaattg catgaattag agctatcacc
                                                                     240
taagtgtggg ctaatgtaac aaagagggat ttcacctaca tccattcagt cagtctttgg
                                                                     300
gggtttaaag aaattccaaa gagtcatcag aagaggaaaa atgaaggtaa tgttttttca
                                                                     360
gactggtaaa gtctttgaaa atatgtgtaa tatgtaaaac attttgacac ccccataata
                                                                     420
tttttccaga attaacagta taaattgcat ctcttgttca agagttccct atcactcttt
                                                                     480
aatcactact cacagtaacc tcaactcctg ccacaatgta caggatgcaa ctcctgtc
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  <213> Artificial Sequence
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С
                                                                      61
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human
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human
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human	Ten primer for ereacting a dominant negative matanic (nite	A, MI4IB, OI						
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human	rek primer for creating a dominant negative mutant (hi40	K, HI4IL) OI						
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400	C.D.							
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